Docket: 399037

REMARKS

Claims 1-7, 14-21, 34-50 are pending in the application. Claims 1-3, 5, 6, 15, 19-21, 39, and 43 are currently amended. Claims 37, 51 and 52 are currently cancelled.

Oath/Declaration

Applicant's attorney attaches a copy of the declaration that was filed in this case with a response to missing parts on May 29, 1998 (Appendix A). This should satisfy the requirement to submit a replacement declaration. Inventor Russell T. Jordan is now deceased.

Claim Amendments

Claim 1 has been amended to clarify that the composition is a pharmaceutical grade material. Claims 2 and 3 have been amended to clarify that the ratio is a molar ratio, as is consistent with the first paragraph of the detailed description. Claim 19 has been amended to recite the antioxidant as a mans, as is consistent with the disclosed embodiments of the specification and the structural equivalents thereof. Claims 20 and 21 have been amended to narrow the list of antioxidants.

Claim Rejections – 35 U.S.C. 112

Claims 20-21 and 51-52 stand rejected for nonenablement. Applicants' attorney respectfully disagrees. Although the list of antioxidants has been narrowed in claims 20 and 21, claim 19 addresses an antioxidant means as is consistent with the disclosure. The teaching is that the ascorbates and NDGA derivatives stabilize the oxine, and this does not require undue experimentation.

Claim Rejections –35 U.S.C. §102

Claims 1 and 2 stand rejected over United States Patent number 4,766,113 issued to West et al. West '113 describes the formulation of a wood-treating product. The Examiner has identified a commercial product that contains 10% copper oxinate, namely, Nylate-10. The EPA registration for this product has been cancelled, but Applicant's attorney submits a Pesticides Database printout (Appendix B) showing the former uses for this product. It was used primarily on wood to prevent rot. This use differs from a pharmaceutical use of what is presently claimed.

Amended claim 1 distinguishes the Nylaate 10 product and West et al. by reciting a pharmaceutical grade material. This term is understood to mean that the claimed material meets the requisite standards for the intended environment of use, as is consistent with the specification (see paragraphs 20 and 44 of the published application). Pharmaceutical use is inapposite to use as a wood preservative. Therefore, claims 1 and 2 are not anticipated.

Claim Rejections—35 U.S.C. §103

Claims 1-7, 14-21, 34-37 and 39-52 stand rejected under 35 U.S.C. §103(a) as being unpatentable over WO 95/03032 to Unilever. Unilever is said to describe the use of a composition comprising 8-hydroxyquinoline and Zn^{2+}; however, the Examiner also explains that Unilever does not show use of at least 5% by weight of these materials. The Examiner asserts that motivation exists to use an increased concentration of 8-hydroxyquinoline and zinc because "the vehicle ranges from 2 to 99%." The examiner argues that the broad range of the vehicle (the carrier) permits selective design of the Unilever formulation to include virtually any amount of 8-hydroxyquinoline and zinc. Unilever fails to specify any particular amounts of 8-hydrozyquinoline and zinc whatsoever.

With all due respect, the rejection does not state a *prima facie* case because Unilever is nonanalogous art. The Unilever composition is a skin treatment agent that is designed to improve the appearance of dry, flaky or aged skin. This has noting to do with a composition for treating cancer, and those skilled in the art would not consult the skin emollient composition art when looking to provide a cancer drug. Unilever is not even reasonably pertinent to Applicants' field of endeavor.

It is also the case that Unilever failed to appreciate that using increased amounts of 8-hydroxyquinoline and zinc, as is claimed, would have an anticancer effect *where also Unilever does not teach supplementation with zinc.* Unilever merely teaches that zinc is to be sequestered—and this is done in-situ with respect to zinc in the native skin. See page 7 at lines 5-15. This teaches away from what is clamed because Unilever teaches the mitigation of native zinc, not supplementation by zinc.

As a further point on this same topic, it will be appreciated that a concentration of zinc chloride (see claim 39) generally above 40% is escharotic (see claim 1). Unilever

teaches a composition to improve the appearance of normal skin, not to chemically burn the skin away. Therefore, Unilever teachers away from what the Examiner proposes as motivation, expressly because the motivation proposed by the Examiner is inapposite to the purpose of the Unilever composition. It would not be possible to use up to 99% zinc oxinate as the Examiner suggests. Actually, this motivation is far beyond Unilever, which does not teach or suggest supplementation with zinc. This shows that the motivation is improperly made in hindsight.

Even assuming arguendo that the Examiner has stated a prima facie case, what is claimed is still patentable.

> When an applicant seeks to overcome a *prima facie* case of obviousness by showing improved performance in a range that is within or overlaps with a range disclosed in the prior art, the applicant must "show that the [claimed] range is critical , generally by showing that the claimed range achieves unexpected results relative to the prior art range."

In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) (citing *In re Woodruff*, 919 F.2d 1575, 1578, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). This is an extension of the *Papesch* doctrine:

> The Hass and Henze cases, which are mentioned, ante- date section 103 and suggest, by way of dicta, that proof of the existence of unobvious or unexpected beneficial properties in a new compound, which would otherwise appear to be obvious (along with its properties), is indicative of the presence of "invention" and hence of patentability. What this comes down to, in final analysis, is a rather simple proposition: If that which appears, at first blush, to be obvious though new is shown by evidence not to be obvious then the evidence prevails over surmise or unsupported contention and a rejection based on obviousness must fall. Many cases, both before and after the enactment of section 103, have been decided according to such reasoning

In re Papesch, 315 F.2d 381, 137 USPQ 43, (CCPA 1963).

It is only fair to say that Unilever and Kolias in combination did not teach, suggest, or even purport to suspect, that use of the claimed range would be useful in the treatment of cancer. This is especially true of what is claimed as the minimum effective amount of 5% capped by a concentration that is not escharotic in healthy tissues. This result in the narrower range is, indeed, unexpected and the range is critical for this purpose.

The Examiner applies Kolias as disclosing that "the ingredients may comprise any amount that is effective and once a composition is known in the art it is within the skill of the artisan to determine optimum amounts and ratios of an ingredient. With all due respect, it is inappropriate to apply Kolias for the purpose of optimizing the skin-conditioner of Unilever. Optimization of the Unilever formulation would have produced an optimized skin conditioner, not an anticancer drug.. This is not a case of routine optimization, especially where Unilever does not teach supplementation with zinc.

For the reasons explained above, Applicants' attorney respectfully requests withdrawal of the §103 rejection.

Therefore, Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. 103.

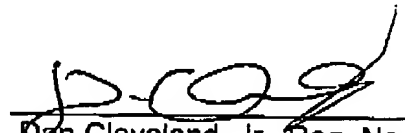
Double Patenting

As the rejection is provisional in nature and the claims of the other application have not been allowed, Applicants must delay the filing of a terminal disclaimer until it is necessary to do so.

The amended claims are patentable for the above reasons. No additional fees are seen to be due. However, if any additional fees are due, the Commissioner is authorized to charge them to deposit account No. 12-600.

Respectfully submitted,

LATHROP & GAGE, LC

By: 

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DECLARATION FOR PATENT APPLICATION

Docket Number: 8020/002

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name. I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled "CHELATED 8-HYDROXYQUINOLINE AND USE THEREOF IN A METHOD OF TREATING EPITHELIAL LESIONS", the specification of which is attached hereto unless the following is checked:
__ was filed on _____ as United States Application Number _____ or PCT International Application Number _____ and was amended on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.
I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56.
I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed.
Prior Foreign Application(s)

(Number)	(Country)	(Day/Month/Year Filed)	Priority Claimed
			__ Yes __ No

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

(Application Number)	(Filing Date)	(Status - patented, pending, abandoned)

I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and to transact all business in the U.S. Patent and Trademark Office connected therewith: Donald M. Duft 17,484; James M. Graziano 28,300; Carl A. Forest 28,494; Mark A. Guetlich 38,900; Dan Cleveland, Jr. 36,106; Michael J. Setter 37,936; William P. Wilbar P43,265; Robert M. Meeks 40,723; and Steven W. Weinrieb 26,520. Address all telephone calls to Dan Cleveland, Jr., at Telephone No. (303) 449-9497 and address all correspondence to Dan Cleveland, Jr., DUFT, GRAZIANO & FOREST, P.C., 1790 - 30th Street, Suite 140, Boulder, Colorado 80301-1018.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of sole or first inventor, if any (given name, family name) Russel T. Jordan, M.D., Ph.D.
Inventor's signature _____ Date 5/23/98
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Inventor's signature _____ Date 5-22-98
Residence Parker, Colorado Citizenship U.S.
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APPENDIX A

PAN Pesticides Database - Pesticide Products

Product Name: Nylate 10-bfg

Note: See Working with the Information on this Page section below for important notes about this data.

Product ID	Identifying information, including U.S. EPA registration number, product registration status, formulation and warning label, as well as links to sources of product labels and MSDS information.
Toxicity	Summary of the toxicity properties of each active ingredient and the percent of each active ingredient in the product.
Uses	Approved uses for the product by general use type, pest, and crop or location.
Registration	Product registration history, including initial date registered, date cancelled (if applicable), and date registration was transferred (if applicable).
Company	Name, address, and identifying number of the company that registered the product. Name and address of the agent, if applicable.
Distributor Names	Complete list of names under which this product is sold. Often a company will register a single product and then sell the same product under many different brand names. The 'Distributor Name' list is a complete list of these names.

Product Identification for Nylate 10-bfg

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Basic Identification Information About This Product

MSDS and Product Label	Select Source
U.S. EPA Product Reg No	35977-16
Product Registration Status	Cancelled
Formulation	Emulsifiable concentrate
Acute Hazard Warning Label	3 Caution
Restricted Use Product	No
PAN Bad Actor Product:	
No. of names this product is sold under	1 (See bottom of page for complete list of products)

Toxicity for Nylate 10-bfg

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Summary Toxicity Information for the Active Ingredients in this Product

For detailed chemical information click on the chemical names below

Active Ingredients Chemical Name	Percent	PAN Bad Actor Chemical [1]	Acute Toxicity [2]	Carcinogen	Cholinesterase Inhibitor	Developmental or Reproductive Toxin	Endocrine Disruptor	Acute Aquatic Toxicity
1. Copper 8-quinolinolate	9.00 %	Not Listed	Not Acutely Toxic	Unclassifiable	No	?	?	

APPENDIX B

Cancellation Date: Oct 10, 1989

Cancel/Transfer Reason: Maint. fee non-payme

Company and Agent Information for Nylate 10-bfg

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Manufacturer	Agent	Distributor
Maag agrochemicals Po box 6430 Vero beach, FL 32961 Phone: 4076677506 Company Number: 035977	No Agent, See Company Info.	No Additional Distributor, See Company Info.

Distributor Names for Nylate 10-bfg

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Product names	Distributor	Product Type	Approval Date	Cancellation Date
Nylate 10-bfg	Maag agrochemicals	Parent Product	Jan 13, 1984	Oct 10, 1989

Working with the Information on this Page

Click on underlined terms for definitions or go to the Pesticide Tutorial overview page.

Any underlined term with a book icon has additional information.

To print this page, choose **Print**. To export this data, choose **Save As** 'HTML Source' and open it in Excel or equivalent program.

APPENDIX B

Indicates high toxicity in the given toxicological category.

Indicates no available weight-of-the-evidence assessment. For additional information on toxicity from scientific journals or registration documents, see the "Additional Resources for Toxicity " section of the chemical detail page for each active ingredient.

1. PAN Bad Actors are chemicals that are one or more of the following: highly acutely toxic, cholinesterase inhibitor, known/probable carcinogen, known groundwater pollutant or known reproductive or developmental toxicant. NOTE! Because there are no authoritative lists of Endocrine Disrupting (ED) chemicals, EDs are not yet considered PAN Bad Actor chemicals.

2. The acute toxicity reported here is for the pure active ingredient only and may not reflect the acute toxicity of individual pesticide products. The acute toxicity of this product can be found in the Product ID section of this page, the Acute Hazard Warning Label.

Other Ingredients in this Product

By U.S. law, only active ingredients (AIs) are reported. In addition to active ingredients, pesticide products may contain one or more "inert" ingredients. Many "inert" ingredients in current use have known adverse human and environmental effects.

U.S. EPA statement on inerts U.S. EPA list of inerts NCAP Inerts Report (pdf)

Historic Uses in the U.S. for Nylate 10-bfg

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Note! This product is now cancelled, when it was registered it was used for the following:

Uses

Fungicide

Pests

Mold/mildew

Crops and Locations

Greenhouse benches (wood) , Wood fences , Wood decks , Wood patios , Wood fences (soil contact nonfumigation treatment) , Wood fences (nonsoil contact nonfumigation treatment) , Wood (construction) (soil contact non-fumigation treatment) , Wood beams (nonsoil contact nonfumigation treatment) , Wood protection trt to finished wood products , Wood frames , Wood millwork , Wood shingles , Wood shingles (roof) Wood picnic tables , Playground equipment (wood)(nonsoil contact nonfumigation treatment) , Wood structural parts (nonsoil contact nonfumigation treatment) , Wood plant stakes , Wood greenhouse flats (soil contact nonfumigation treatment) , Wood mushroom trays (soil contact nonfumigation treatment) , Wood protection trt to wooden food/feed containers , Wood produce containers , Wood interior walls/floors (wheeled vehicles) , Wood interior components (refrigerators/walk-in cold storage units) , Wood boat holds (interior) , Wood swimming pool walks , Wood cases , Wood pressure treatment , Wood components (showers/bathrooms) , Cooling tower wood , Rope , Textiles (cotton) , Cotton rope , Cotton duck , Cotton webbing , Wood surfaces , Wood surfaces (outdoor)

U.S. Product Registration History for Nylate 10-bfg

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U.S. EPA Product Reg No: 35977-16 U.S. State Registration Searches

Product Registration Status: Cancelled

Approval Date: Jan 13, 1984